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MEDICINAL PLANTS IN THE MANAGEMENT OF ANXIETY DISORDERS: MECHANISMS, THERAPEUTIC POTENTIAL AND CLINICAL PERSPECTIVES

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Abstract

Anxiety disorders are among the most prevalent psychiatric illnesses worldwide and represent a significant public health concern due to their high prevalence, chronic nature, and substantial impact on quality of life. These disorders encompass a broad spectrum of conditions, including generalized anxiety disorder, panic disorder, social anxiety disorder, specific phobias, agoraphobia, separation anxiety disorder, and selective mutism. The pathophysiology of anxiety involves complex interactions among neurotransmitter systems, particularly gamma-aminobutyric acid (GABA), serotonin, dopamine, and norepinephrine, along with dysfunction of brain regions such as the amygdala, hippocampus, and prefrontal cortex. Although conventional pharmacological therapies, including benzodiazepines, antidepressants, and monoamine oxidase inhibitors, are effective in managing anxiety symptoms, their long-term use is often associated with adverse effects, tolerance, dependence, and withdrawal complications. Consequently, there has been increasing interest in medicinal plants and herbal formulations as safer and more accessible alternatives. Numerous medicinal plants, including *Nigella sativa*, *Passiflora incarnata*, *Bacopa monnieri*, *Withania somnifera*, *Eschscholzia californica*, *Tinospora cordifolia*, *Ziziphus jujuba*, *Crocus sativus*, *Rubus brasiliensis*, and *Euphorbia hirta*, have demonstrated significant anxiolytic activity through modulation of GABAergic, serotonergic, antioxidant, and anti-inflammatory pathways. This review highlights the epidemiology, classification, pathophysiology, conventional treatment approaches, and therapeutic potential of medicinal plants in anxiety management. The available evidence suggests that herbal medicines may serve as promising complementary or alternative therapeutic options for anxiety disorders, warranting further pharmacological and clinical investigations.

Keywords: Anxiety Disorders; Medicinal Plants; Herbal Medicine; Anxiolytic Activity; *Nigella sativa*; *Passiflora incarnata*; *Bacopa monnieri*; *Withania somnifera*; GABAergic System; Neurotransmitters; Phytotherapy; Mental Health; Natural Products; Complementary Medicine.

Introduction

Anxiety

According to the World Health Organization, anxiety disorders are burdensome "common mental disorders" to communities. These prevalent disorders are not communicable and affect approximately one in every five individuals of the world population. This figure represents the largest share of the prevalence of all mental disorders, whereas severe psychotic and bipolar disorders affect only between 1% and 2% of the population. In an upper-middle income country such as Brazil, the 12-month prevalence of anxiety disorders has been estimated as 19.9% among the dwellers of a large metropolitan area.

The cost of anxiety disorders to the working world is remarkable, corresponding to a total loss of 74.4 billion Euros in 2010. The global burden of anxiety disorders represents 10.4% of years lived with adjusted disability (DALY) of mental disorders, reaching 26,800,000 DALYs. Despite the societal burden of this morbidity, only approximately one in five patients diagnosed with anxiety disorder obtain access to treatment (Whiteford *et al*., 2010; Wittchen *et al*., 2011).

Similar to depression, anxiety disorders are among the most common psychiatric conditions. They include a diverse spectrum of illnesses. The majority of anxiety disorders initially manifest in adolescence and childhood. Research indicates that a significant number of kids do not overcome their anxiety disorders as they enter adolescence or adulthood. Anxiety disorders have a lifetime prevalence rate of 24.9%. According to this data, anxiety disorders appear to be more chronic than affective or drug-related disorders. The prevalence of anxiety disorders is hard to determine because results can be affected by even slight modifications to diagnostic criteria, interview questions, or study design (Stavrakaki and Vargo, 1986).

Types of anxiety

GAD

This chronic disorder involves excessive, long lasting anxiety and worries about nonspecific life events, objects, and situations. GAD is the most common anxiety disorder, and people with it are not always able to identify the cause of their anxiety.

Agoraphobia

This is a fear and avoidance of places, events, or situations from which it may be difficult to escape or where help would not be available in emergencies.

People often misunderstand this condition as a phobia of open spaces and the outdoors. A person with agoraphobia may fear leaving home or using elevators and public transport (Sarkar, 2020).

Selective mutism

Some children experience this form of anxiety, in which they cannot speak in certain places or contexts, even though they may have excellent verbal communication skills around familiar people.

Social anxiety disorder

This is a fear of adverse judgment from others in social situations or of public embarrassment. Social anxiety disorder includes a range of feelings, such as stage fright, a fear of intimacy, and anxiety around humiliation and rejection.

Panic disorder

Brief or sudden attacks of intense terror and apprehension characterize panic disorder. These attacks can lead to shaking, confusion, dizziness, nausea, and breathing difficulties. Panic attacks tend to occur and escalate rapidly. Panic disorders usually occur after frightening experiences or prolonged stress but may also occur without a trigger.

Specific phobia

This is a fear and avoidance of a particular object or situation. Phobias are not like other anxiety disorders, as they relate to a specific cause. A person with a phobia might acknowledge fear as illogical or extreme but remain unable to control feelings of anxiety around the trigger. Triggers for a phobia range from situations and animals to everyday objects.

Separation anxiety disorder

High anxiety levels after separation from a person or place that provides feelings of security or safety characterize separation anxiety disorder. Separation anxiety is most

common in young children but can affect people of all ages (Finlay-Jones and Brown, 1981; Hughes *et al*., 2006).

Causes

- **Environmental stress**. This refers to stressful events you have seen or lived through. Life events often linked to anxiety disorders include childhood abuse and neglect, a death of a loved one, or being attacked or seeing violence.
- **Drug withdrawal or misuse**. Certain drugs may be used to hide or decrease certain anxiety symptoms. Anxiety disorder often goes hand in hand with alcohol and substance use.
- **Medical conditions**. Some heart, lung, and thyroid conditions can cause symptoms similar to anxiety disorders or make anxiety symptoms worse. It's important to get a full physical exam to rule out other medical conditions when talking to your doctor about anxiety
- **Genetics**. Anxiety disorders can run in families.
- **Brain chemistry**. Some research suggests anxiety disorders may be linked to faulty circuits in the brain that control fear and emotions (Bateson *et al*., 2011; Somers *et al*., 2006).

Pathophysiology of anxiety

Anxiety and the potential health problems it can bring on are theorized to have their origins in central nervous system modulation issues.

Anxiety disorders have been linked to the chronic dysregulation of brain networks, including cortical and subcortical areas, and this has been observed in animals and humans (amygdala, hippocampus, thalamus, prefrontal, and cingulate cortex). Weaker inhibitory GABAergic transmission in the brain has been linked to anxiety. Ligands regulate chloride selectivity at the GABAA receptor.

The protein consists of five different subunits that form a heterooligomer and can traverse the neuronal membrane. Most GABAA receptors have a trimeric structure with two identical subunits and a single, non-identical subunit. The subunit increases the likelihood of channel opening in response to GABA by interacting inside the interface between the subunits, whereas the subunit allows GABA binding and confers sensitivity to benzo[a]pyrene (BZD).

At least two GABA molecules are required to activate this chloride/bicarbonate-permeable channel, inducing an inflow of negatively charged chloride ions and temporarily reducing the neuron's ability to generate action potentials, resulting in phasic inhibition. Drugs that bind to the GABAA receptor have an anxiolytic effect via enhancing GABA's neuronal inhibitory effects by facilitating chloride channel opening.

Treatment

Medications

A person can support anxiety management with several types.

Medicines that might control some physical and mental symptoms include antidepressants, benzodiazepines, and tricyclic antidepressants.

Benzodiazepines: A doctor may prescribe these for certain people with anxiety, but they can cause addiction. Diazepam, or Valium, is a common benzodiazepine.

Antidepressants: These commonly help with anxiety, even though they also target depression. Serotonin reuptake inhibitors (SSRIs), fluoxetine, and citalopram are examples.

Tricyclic antidepressants: These are an older class of drugs that benefit most anxiety disorders other than obsessive-compulsive disorder (OCD). Imipramine and clomipramine are two examples of tricyclics.

Additional drugs a person might use to treat anxiety include:

Monoamine oxidase inhibitors (maois)

Beta-blockers

Buspirone (Allen *et al*., 1995; Bandelow *et al*., 2015).

Self-treatment

Sometimes, a person can treat an anxiety disorder at home without clinical supervision. However, this may not be effective for severe or long-term anxiety disorders.

There are several exercises and actions to help a person cope with milder, more focused, or shorter-term anxiety disorders, including:

- stress management
- relaxation techniques

- maintaining support networks
- physical exercise

Counselling

A standard way of treating anxiety is psychological counseling. This can include cognitive behavioral therapy (CBT), psychotherapy, or a combination of therapies

CBT is a type of psychotherapy that aims to recognize and change harmful thought patterns that form the foundation of anxious and troublesome feelings (Ballenger, 1999; Nutt, 2005).

Due to side effects and destructive effects of some chemical drugs, many patients prefer herbal medicines to treat diseases. Although there are key review papers in the area of medicinal plants and psychiatry disorders, they have either covered the area in a relatively cursory manner or focused on a specific plant medicine. In the present study, we tried to present the effect of most important medicinal plants on two important highly comorbid psychiatric conditions-anxiety and depression.

From a sample size of more than 2 000 subjects interviewed during 1997-1998, it was estimated that more than half of those suffered anxiety attacks, and more than 54% of those with severe depression had used medicinal plants or other complementary therapies during the previous 12 months to treat their disorders. The inpatients hospitalized for acute care of various psychiatric disorders in North America also showed that 44% had used herbal medicines during the previous 12 months for psychiatric purposes. About 25% of all drugs prescribed by doctors in the current medicine are obtained from herbs in different forms. Some of them are produced directly from plant extracts and others are produced artificially to provide effects similar to herbal drugs. Over the last two centuries, with the isolation of active constituents, such as morphine from opium poppies, recognition of psychoactive plants has significantly advanced, and various kinds of researches on herbal medicine have increased in recent years with more than 50% increase in the literature over 5 years up to 2008 (Khan *et al*., 2022; Fajemiroye *et al*., 2016).

Herbal medicine

The world health organization describes mental health as a state of emotional and psychological well-being that enables individuals to meet the demands of everyday life, function in society, use their cognitive and emotional abilities effectively, and

develop fulfilling, mature relationships. It also comprises the ability to adjust to both internal problems and external situations, as well as to productively engage in social development.

A long-standing concept in ayurveda and traditional medicine, polyherbalism is predicated on the idea that combining herbs with complementary actions produces better therapeutic benefits than a single agent, simultaneously addressing oxidative stress, modulating neurotransmitter systems, and reducing inflammatory reactions. Carefully A long-standing concept in ayurveda and traditional medicine, polyherbalism is predicated on the idea that combining herbs with complementary actions produces better therapeutic benefits than a single agent, simultaneously addressing oxidative stress, modulating neurotransmitter systems, and reducing inflammatory reactions. Particularly designed polyherbal mixtures may be used as multipleacting treatments for anxiety, according to recent preclinical research. This approach is used in the current study, which employs three plants with established neuroprotective qualities: passiflora incarnate,nigella sativa,bacopa monnier etc (Borrás *et al*., 2021).

General Mechanism Of Action Of Anxiety

Anti-anxiety herbal plants

Nigella sativa

A Black Cumin is a medicinal herbal plant belonging to the family Ranunculaceae . The plant's seeds have long been used in various medical contexts. It has been widely utilized to treat disorders of the nervous system, including pain, brain injury, sleeping disorders, impairment of memory, and more. Furthermore, it is found that thymoquinone (TQ), a significant bioactive constituents of the essential oil, is reliable for much of the plant's medicinal qualities (Butt and Sultan, 2010).

Figure 1: ***Nigella sativa***

Passiflora incarnate

Passiflora incarnate known as passionflower belonging to family passifloraceae, P. incarnata is recognised as a plant medication. According to reports, P. incarnata's primary phytoconstituents are flavonoids. Among these are kaempferol and quercetin. The primary bioactive phytoconstituents of Passiflora incaranata have been proposed to be the harman alkaloids, the flavonoid chrysin, because of their ability to inhibit the MAO enzyme. According to recent findings, the body's benzodiazepine and GABA receptor-mediated biochemical processes are reliable for the sedative & anxiolytic activities of passiflora incarnate (Miroddi *et al*., 2013).

Figure 2: ***Passiflora incarnate***

Bacopa monnieri

The Ayurvedic medicine Bacopa monnieri, commonly known as Brahmi, is a member of the Plantaginaceae family. is utilised as an anxiolytic and nootropic. Through GABAergic, antioxidant, and antiinflammatory effects, its active bacosides protect the brain without inducing amnesia, improve memory, intelligence, and brain function, and lessen stress and anxiety (Aguiar and Borowski, 2013).

Figure 3: ***Bacopa monnieri***

Withania somnifera

withania somnifera ia a traditional ayurvedic herb known as an adaptogen belonging family solanaceae ayurvedic medicine for its calming,stress-reducing.

Figure 4: ***Withania somnifera***

Eschscholzia californica

Eschscholzia californica, commonly known as the California poppy, is a small herbaceous plant belonging to the poppy family. It is characterized by blue-green, finely divided leaves and bright orange, cup-shaped flowers that close at night or during cloudy conditions. Native to western North America, the plant thrives in sunny, dry environments with poor, well-drained soil and is recognized as the state flower of California (Rolland *et al*., 1991).

Figure 5: ***Eschscholzia californica***

Tinospora cordifolia

In Ayurveda, Tinospora cordifolia also referred to as Guduchi or Giloy is a significant medicinal plant. By soothing the neurological system, it is used to reduce tension and anxiety. Through the balance of brain chemicals, the plant exhibits anti-anxiety

(anxiolytic) activity. Proteins, alkaloids, flavonoids, and saponins are examples of active ingredients. Saponins and flavonoids primarily aid in lowering tension and anxiety. Additionally, guduchi enhances mental health and immunity (Saha and Ghosh, 2012).

Figure 6: *Tinospora cordifolia*

Ziziphi Jujubae

The botanical source of Semen Ziziphi Jujubae (Suanzaoren), the dried seeds commonly used in Chinese medicine to alleviate palpitations, anxiety, and insomnia, is Ziziphus jujuba, a member of the Rhamnaceae family. Jujubosides (A and B), flavonoids, and alkaloids are among the bioactive components of the seeds that contribute to its sedative and anxiolytic properties. According to pharmacological research, the extract modulates the GABAergic and monoaminergic neurotransmitter systems to generate sedative effects at higher dosages and anxiolytic activity at lower concentrations (Mahajan *et al*., 2009).

Figure 7: *Ziziphi Jujubae*

Crocus sativus

Saffron, scientifically known as Crocus sativus L., belongs to the Iridaceae family. It is obtained from the dried stigmas of the Crocus sativus flower, a perennial plant cultivated in regions such as Iran, India, and the Mediterranean. Key bioactive compounds present in saffron include crocin, crocetin, safranal, and picrocrocin. Among these, crocin and safranal are primarily in charge of its anti-anxiety actions because they elevate mood and have a relaxing influence on the neurological system (Srivastava *et al*., 2010).

Figure 8: ***Crocus sativus***

Rubus brasiliensis

Rubus brasiliensis, originating from Brazil, belongs to the Rosaceae family and is commonly utilized in traditional medicinal practices. Research indicates that its waxy ethanolic extract and infusion have anxiolytic effects on mice and rats. The active substances are probably lipid-soluble components that influence the GABA A.The -benzodiazepine receptor system, which is comparable to popular anxiety medications and has little acute toxicity (Bueno *et al*., 2021).

Figure 9: ***Rubus brasiliensis***

Euphorbia hirta

Euphorbia hirta, belonging to the Euphorbiaceae family, is a medicinal herb. This small, hairy plant, widespread in tropical regions, is used as the source for various biological remedies.Flavonoids, tannins, phenolic compounds, alkaloids, and triterpenoids are among its significant chemical components. According to studies, Euphorbia hirta has anti-anxiety activity mostly because of its flavonoids, which act on brain receptors linked to stress and anxiety to help calm the nervous system (Kumar *et al*., 2010).

Figure 10: ***Euphorbia hirta***

Conclusion

Anxiety is an ordinary, yet profoundly abstract, human feeling. While anxiety fills a valuable and versatile need, anxiety can likewise turn into the reason for suffering over huge number of individuals. Working from a biopsychosocial point of view, this article gave an outline of the root and useful motivation behind anxiety. The natural, mental, and social factors that add to the arrangement and upkeep of (neurotic) anxiety issues were introduced. The different anxiety problems, speculations, and related medicines were looked into. The treatment for tension issues depends on a strong logical establishment, grounded in examination by specialists from different fields. The examination has explored these organic, social, and mental elements that add to tension problems. This wide exploration base has prompted the improvement of various, exactly based medicines that have demonstrated to be profoundly viable. Thus, a great many people have recovered their health, reestablished their working, and now appreciate lavishly fulfilling and fulfilling lives. The future remaining parts increases hopes for the individuals who battle with anxiety. We are sure that progressions in the treatment of anxiety problems will keep on carrying expectation and help to the individuals, and families, influenced by these issues.

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